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Original Article

A focussed single-view hand-held echocardiography protocol for the detection of rheumatic heart disease

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Abstract *Background:* Echocardiographic screening represents an opportunity for reduction in the global burden of rheumatic heart disease. A focussed single-view screening protocol could allow for the rapid training of healthcare providers and screening of patients. *Objective:* The aim of this study was to determine the sensitivity and specificity of a focussed single-view hand-held echocardiographic protocol for the diagnosis of rheumatic heart disease in children. *Methods:* A total of nine readers were divided into three reading groups; each interpreted 200 hand-held echocardiography studies retrospectively as screen-positive, if mitral regurgitation ⩾1.5 cm and/or any aortic insufficiency were observed, or screen-negative from a pooled study library. The performance of experts receiving focussed hand-held protocols, non-experts receiving focussed hand-held protocols, and experts receiving complete hand-held protocols were determined in comparison with consensus interpretations on fully functional echocardiography machines. *Results:* In all, 587 studies including 76 on definite rheumatic heart disease, 122 on borderline rheumatic heart disease, and 389 on normal cases were available for analysis. The focussed single-view protocol had a sensitivity of 81.1%, specificity of 75.5%, negative predictive value of 88.5%, and a positive predictive value of 63.2%; expert readers had higher specificity (86.1 versus 64.8%, $p < 0.01$) but equal sensitivity. Sensitivity – experts, 96% and non-experts, 95% – and negative predictive value – experts, 99% and non-experts, 98% – were better for definite rheumatic heart disease. False-positive screening studies resulting from erroneous identification of mitral regurgitation and aortic insufficiency colour jets increased with shortened protocols and less experience ($p < 0.01$). *Conclusion:* Our data support a focussed screening protocol limited to parasternal long-axis images. This holds promise in making echocardiographic screening more practical in regions where rheumatic heart disease remains endemic.

Keywords: Rheumatic heart disease; hand-held echocardiography; task shifting

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Rheumatic heart disease is the most common cause of acquired cardiovascular disease in children and young adults in the world today, affecting 32.9 million persons and causing 345,000 deaths annually.[1,2] A recent multinational registry in low- and middle-income countries showed that most rheumatic heart disease patients have advanced disease (63.9%) and complications at the time of diagnosis, as well as a high (16.9%) 2-year case fatality rate[3,4]; however, rheumatic heart disease is a cumulative process and opportunities do exist for early intervention in childhood.

Echocardiographic screening may represent an opportunity for reduction in the global burden of

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‡The original version of this article was published with an error in one of the author names. A notice detailing this has been published and the error rectified in the online and print PDF and HTML copies.

rheumatic heart disease by identifying children at the earliest stages of the disease who are candidates for penicillin prophylaxis[5–8]; however, endemic rheumatic heart disease is most common in low-resource settings, home to over two billion children, where human and financial resources are severely constrained.[1] Use of hand-held echocardiography equipment reduces costs and has reasonable sensitivity and specificity.[9–11] Shifting screening tasks to non-physician healthcare workers shows promise towards developing a practical workforce.[9,12] Both are improved further through the implementation of simplified protocols that save time and require less expertise and training[13]; however, sustainability of these strategies deployed as vertical programmes, focussed just on rheumatic heart disease screening, is unlikely.

The diagonal integration of echocardiographic screening for rheumatic heart disease into existing primary healthcare settings may provide a more sustainable platform for rheumatic heart disease screening in low- and middle-income countries. Such integration will face the challenge of feasibility and prioritisation within an often overly busy clinical environment. In addition, integrative programmes will require training of a diverse and often rapidly changing group of providers with different medical backgrounds and knowledge of cardiac anatomy. In this unique setting, a highly simplified rheumatic heart disease screening protocol, focussed on education on acquiring the shortest and most reproducible set of images, could overcome these barriers, allowing for rapid training of healthcare providers and rapid screening of patients. A protocol limited to obtaining parasternal long-axis images using hand-held echocardiography has the potential to fulfil this need.[14,15]

The primary aim of this study was to determine the sensitivity, specificity, positive predictive value, and negative predictive value of a focussed single-view hand-held echocardiographic protocol – that is, parasternal long-axis – and a single measurement – that is, mitral regurgitation length – for the screening of rheumatic heart disease. We hypothesised that this focussed protocol would have acceptable specificity (>80%) and sensitivity comparable to the current gold standard: imaging using fully functional standard echocardiography machines, as per the 2012 World Heart Federation criteria (Table 1) that include multiple views and spectral Doppler.[16] Secondary aims included comparison of the complete hand-held with the focussed hand-held protocol, comparison of the performance between expert and non-expert readers, comparison of the performance of the hand-held protocol between high- and low-prevalence populations, and the determination of more stringent cut-off points for mitral regurgitation length.

Methods

We conducted a retrospective search of our de-identified image library for paired echocardiograms obtained at the same encounter using standard portable

Table 1. Source of data methodology.

Title	The utility of handheld echocardiography for early diagnosis of rheumatic heart disease[19]	The utility of handheld echocardiography for early rheumatic heart disease diagnosis: a field study[20]	Handheld echocardiographic screening for rheumatic heart disease by non-experts[12]	Efficacy of a standardized computer-based training curriculum to teach echocardiographic identification of rheumatic heart disease to nonexpert users[13]
Purpose of study	Validation of HHE in "spiked" population	Field validation of HHE	Task shifting of HHE to nurses	Computerised training of non-physicians to perform HHE
Who performed HHE?	Cardiologist (US)	Cardiologists (US and Ugandan) Sonographers (US)	Nurses (Ugandan)	Nurses (Brazilian) Technicians (Brazilian)
Who performed full studies?	Cardiologist (US)	Cardiologists (US and Ugandan) Sonographers (US)	Cardiologists (US and Ugandan)	Cardiologists (US and Brazilian)
Who interpreted full studies?	Cardiologists (US and Ugandan) Two reviewers (third if disagreement)	Cardiologists (US and Ugandan) Two reviewers (third if disagreement)	Cardiologists (US and Ugandan) Two reviewers (third if disagreement)	Cardiologists (US and Brazilian) Two reviewers (third if disagreement)
Location	Uganda	Uganda	Uganda	Brazil
Year	2014	2015	2015	2016
Study volume				
Definite RHD	25	47	11	6
Borderline RHD	16	133	32	47
Normal	84	1234	913	336

HHE = hand-held echocardiography; RHD = rheumatic heart disease; US = United States.

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echocardiography (Vivid Q; General Electric, Milwaukee, Wisconsin, United States of America or CX50; Philips, Bothell, Washington, United States of America) and hand-held echocardiography (General Electric VScan, Milwaukee, WI, United States of America). All echocardiograms were obtained as part of previous IRB-approved research studies on children aged 7–18 in Uganda or Brazil with rheumatic heart disease, previously diagnosed using the gold standard of blinded expert consensus interpretation of standard portable echocardiography images as per the 2012 World Heart Federation Criteria.[12,13,19,20] Details on the methodology and level of training is provided in each of the four references and summarised in Table 1.

Corresponding hand-held echocardiography studies were collected and two versions were saved: complete hand-held echocardiography studies, with parasternal long-axis two-dimensional and colour, parasternal short-axis two-dimensional and colour, apical four-chamber two-dimensional and colour, and apical five-chamber two-dimensional and colour images; and focussed hand-held echocardiography, with parasternal long-axis two-dimensional and colour images. A total of 600 unique hand-held echocardiography studies were then randomly allocated using the standard portable echocardiography category to one of three image groups: groups A and B with 100 cases of rheumatic heart disease – of which 40 were definite and 60 were borderline – and 100 normal cases, and group C with 10 rheumatic heart disease cases – of which four were definite and six were borderline – and 190 normal cases. Group C was added to assess performance under "real world" prevalence conditions.

All readers were blinded to clinical and demographic data, consensus standard echocardiography interpretations, and to the interpretations of others within their group. A total of three readers were assigned to each image group from A to C including one expert – reading group 1 – and one non-expert – reading group 2 – receiving the focussed hand-held image protocol and one expert – reading group 3 – receiving the complete hand-held image protocol (Fig 1). Expert readers consisted of six international cardiologists with experience in rheumatic heart disease and the 2012 World Heart Federation criteria (United States of America: C.S., A.B.; Brazil: A.D., M.C.P.N.; Uganda: T.A., E.O.). Non-experts were Brazilian rheumatic heart disease outreach team members comprising two bio-technicians, C.O. and L.X., with 18 months of practical experience and one nurse with 12 months of practical experience, K.O., with 12–18 months of practical experience in echocardiographic screening and interpretation of rheumatic heart disease. Each trainee had received field training from a cardiologist after participating in education based on the same computerised curriculum that was translated into Portuguese (WiRED International http://www.wiredhealthresources.net/EchoProject/index.html). Readers were instructed to identify studies that were not interpretable based on inadequate number of images or poor image quality, and these were excluded from further analyses.

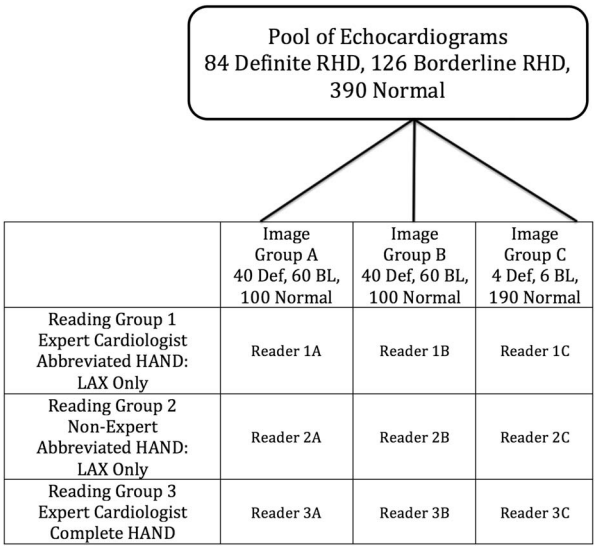

Figure 1.
Study composition showing reading and image groups. BL = borderline; DEF = definite; HAND = hand-held echocardiography; LAX = parasaternal long axis; RHD = rheumatic heart disease.

A randomly sorted image library was created for each reader and distributed on individual flash drives. Readers were blinded to the proportion of rheumatic heart disease cases within their group and to the gold standard rheumatic heart disease diagnosis. Each reader was provided VScan Gateway software (GE) for image interpretation and access to the REDCap electronic data management tool to record their interpretations.[18] Readers were asked to note mitral regurgitation $\geqslant$1.5 cm, mitral regurgitation $\geqslant$2.0 cm, and/or any aortic insufficiency, as has been described in previous studies of simplified rheumatic heart disease diagnostic criteria.[9,10,13]

All data were analysed using MedCalc for Windows 7 version 12.2.1.0 (MedCalc Software, Ostend, Belgium). A sample size of 200 studies – 100 positive and 100 negative in groups A and B – was chosen based on previously reported sensitivity and specificity data from simplified protocols, to bracket overall 95% confidence intervals (CI) by 10%. As noted above, group C was included to represent "real world" prevalence of rheumatic heart disease.

The individual and pooled sensitivity, specificity, positive predictive value, and negative predictive value of experts and non-experts – groups 1 + 2 – receiving focussed hand-held protocols, and experts receiving complete hand-held protocols – group 3 – were calculated and compared using Fisher's exact test.

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Hand-held echocardiography studies were considered screen-positive if readers noted mitral regurgitation ⩾1.5 cm and/or any aortic insufficiency. Similar analyses were performed for comparison of artificial high-prevalence groups – image groups A + B – with the "real world" prevalence group – image group C. The more stringent screen-positive criteria of mitral regurgitation ⩾2.0 cm and/or any aortic insufficiency were considered separately. Reasons for non-agreement for each pooled group, based on standard echocardiographic diagnosis of any rheumatic heart disease versus hand-held echocardiography criteria of mitral regurgitation ⩾1.5 cm or any aortic insufficiency, were reported as percentage by each category for false-positive and negative reads. A p-value of <0.05 was considered significant.

Results

Readers indicated that eight studies had insufficient image quality for interpretation and that five studies had incomplete data in the complete protocol versions; these 13 studies were excluded from further analyses. This left 587 studies, of which 76 were on definite rheumatic heart disease, 122 on borderline rheumatic heart disease, and 389 were on normal cases, or 1761 interpretations – three per study – for analysis. Figure 2a and b serve as examples of mitral regurgitation and aortic insufficiency seen on hand-held parasternal long-axis images. Overall, the focussed single-view protocol of reading groups 1 and 2 with observations of mitral regurgitation ⩾1.5 cm and/or any aortic insufficiency performed reasonably well compared with the gold standard of imaging and interpretation using standard echocardiography based on the 2012 World Heart Federation criteria, with a sensitivity of 81.1% (95% CI 76.9–84.8%), specificity of 75.5% (95% CI 72.3–78.4%), negative predictive value of 88.5% (95% CI 86.2–90.4%), and positive predictive value of 63.2% (95% CI 60.1–66.3%). There was some heterogeneity between the performances of individual readers (Fig 3), with expectedly wide confidence intervals in image group C in which the was a low prevalence of rheumatic heart disease.

Expert and non-expert readers had equal sensitivity for determining if a study in the focussed protocol was screen-positive (77.3 versus 84.8%, p = 0.07); however, experts showed higher specificity for discernment of screen-negative studies (86.1 versus 64.8%, p < 0.01) (Fig 4). There was no difference in sensitivity between experts reviewing the complete hand-held protocol and expert and non-expert review of the focussed hand-held protocol (80.3 versus 81.1%, p = 0.83). The complete hand-held protocol showed better specificity (90.0 versus 75.4%, p < 0.01) though the majority of that difference was attributable to the lower specificity of non-expert readers, with no difference in specificity between experts reading the complete versus the focussed hand-held protocol (90.0 versus 86.1%, p = 0.12).

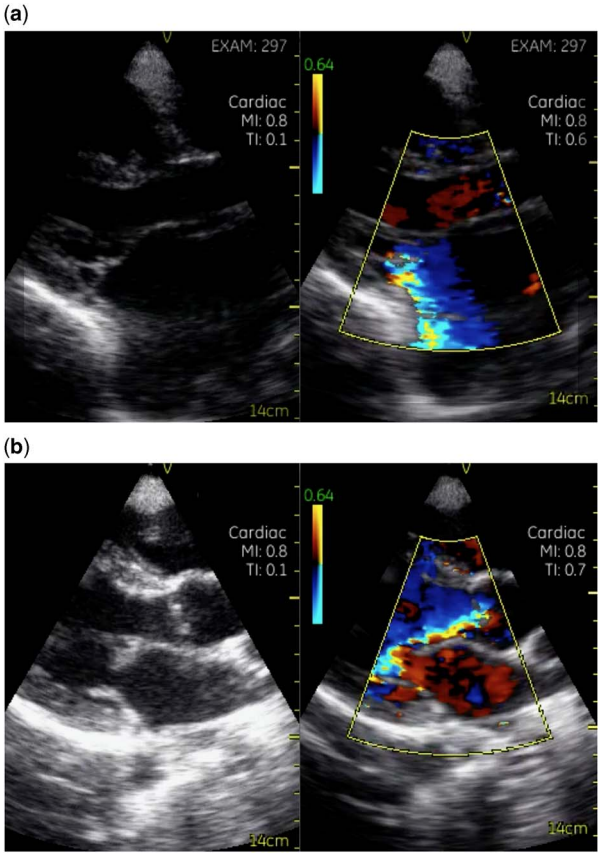

Figure 2.
*(**a**) Black and white (left) and colour (right) parasternal long-axis hand-held echocardiography images of a patient with definite rheumatic heart disease. The mitral regurgitation jet is clearly seen in blue in the colour image. (**b**) Black and white (left) and colour (right) parasternal long-axis hand-held echocardiography images of a patient with definite rheumatic heart disease. The aortic regurgitation jet is clearly seen in blue in the colour image.*

The negative predictive value of the screen-negative study was equal between expert and non-expert readers using the focussed protocol (88.1 versus 89.0%, p = 0.81); however, the positive predictive value of a screen-positive study was higher for experts than non-experts using the focussed protocol (74.2 versus 55.8%, p < 0.01) (Fig 4). There was no difference in the negative predictive value of a study found to be negative by experts using the complete hand-held protocol and a study found to be negative by experts and non-experts using the focussed hand-held protocol (89.0 versus 88.4%, p = 0.48). The positive predictive value of a study found to be positive by experts using the complete hand-held protocol was higher than the positive predictive value of a study found to be positive by experts and non-experts using the focussed hand-

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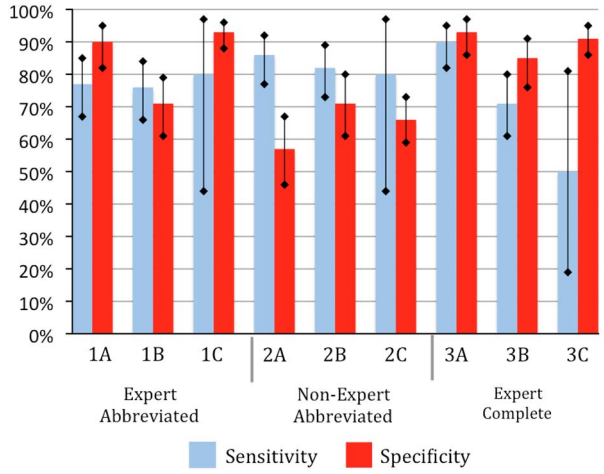

Figure 3.
Performance of individual readers in identifying ANY rheumatic heart disease including definite and borderline rheumatic heart disease according to World Heart Federation criteria. AI = aortic insufficiency; HAND = hand-held echocardiography; MR = mitral regurgitation; RHD = rheumatic heart disease; STAND = standard portable echocardiography.

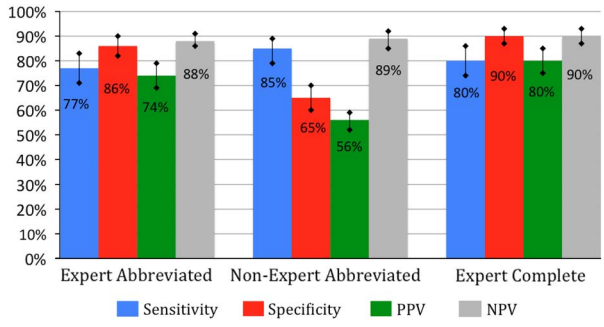

Figure 4.
Performance of pooled reading groups for identifying ANY rheumatic heart disease including definite and borderline rheumatic heart disease according to World Heart Federation criteria. AI = aortic insufficiency; HAND = hand-held echocardiography; MR = mitral regurgitation; NPV = negative predictive value; PPV = positive predictive value; RHD = rheumatic heart disease; STAND = standard portable echocardiography

held protocol (80.3 versus 63.2%, $p < 0.01$), though the majority of that difference was attributable to the positive predictive value of non-expert readers, with no difference in positive predictive value between experts reading the complete versus the focussed hand-held protocol (80.3 versus 74.2%, $p = 0.16$).

Sensitivity for the detection of definite rheumatic heart disease (Fig 5) was higher than that for borderline rheumatic heart disease in all reading groups. Experts who were given the complete hand-held protocol had 100% sensitivity for detecting definite rheumatic heart disease. Sensitivity for detection of definite rheumatic heart disease for experts (96%) and

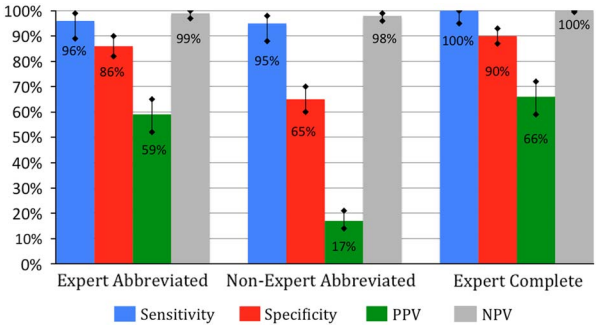

Figure 5.
Performance of pooled reading groups for identifying DEFINITE rheumatic heart disease according to World Heart Federation criteria. AI = aortic insufficiency; HAND = hand-held echocardiography; MR = mitral regurgitation; NPV = negative predictive value; PPV = positive predictive value; RHD = rheumatic heart disease; STAND = standard portable echocardiography.

non-experts (95%) using the focussed hand-held protocol was not significantly different from that of experts using the complete hand-held protocol ($p = 0.25$ and $p = 0.12$, respectively).

The negative predictive value of a screen-negative study for definite rheumatic heart disease was higher than that for borderline rheumatic heart disease, approaching 100% among all reading groups (Fig 5). As expected, based on lower prevalence, the positive predictive value was lower for definite rheumatic disease than for borderline rheumatic disease. The positive predictive value of a study for definite rheumatic heart disease interpreted as screen-positive by non-experts and experts using the focussed hand-held protocol was significantly lower than that for experts using the complete hand-held protocol (66.1 versus 44.3%, $p < 0.01$), though the majority of that difference was attributable to the positive predictive value for definite rheumatic heart disease of a screen-positive study by non-expert readers, with no difference in positive predictive value observed between experts reading the complete versus the focussed hand-held protocol (66.1 versus 58.6%, $p = 0.24$).

The performance of the focussed protocol for detection of rheumatic heart disease was compared between image group C, which was designed to reflect prevalence conditions in the field, and the artificial high-prevalence image groups A + B: 50% in order to carry out power sensitivity and specificity analyses. There was no difference in sensitivity for any rheumatic heart disease (80.0 versus 81.1%, $p = 1.0$) or for a definite rheumatic heart disease (100 versus 95.1%, $p = 1.0$), but group C showed higher specificity than group A + B (79.0 versus 71.9%, $p = 0.025$) (Fig 6). The negative predictive value of the screen-negative study for any rheumatic heart disease was higher for group C than for group A + B

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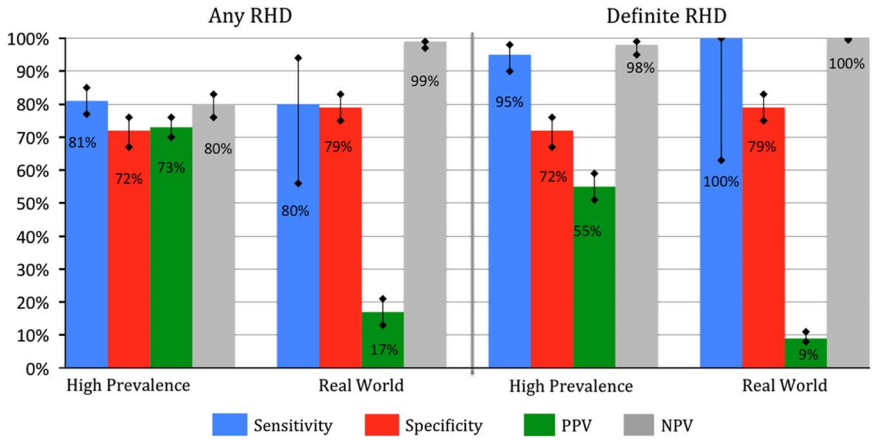

Figure 6.
Performance of pooled artificially high-prevalence and "real world" image groups in identifying ANY rheumatic heart disease including definite and borderline rheumatic heart disease according to World Heart Federation criteria and DEFINITE rheumatic heart disease. AI = aortic insufficiency; MR = mitral regurgitation; NPV = negative predictive value; PPV = positive predictive value; RHD = rheumatic heart disease.

(98.7 versus 80.1%, $p < 0.01$), supporting the value of a screen-negative study using the focussed hand-held protocol under field conditions. The positive predictive value was much lower in group C, as expected with a lower prevalence of rheumatic heart disease in this group.

The use of more stringent criteria for a screen-positive study, of mitral regurgitation ⩾2.0 cm and/or any aortic insufficiency, significantly decreased sensitivity in all groups: between 11 and 19% reduction, $p < 0.01$ for all. In contrast, specificity significantly increased with more stringent criteria: between 6 and 10% increase, $p < 0.01$ for all.

Identification of erroneous colour jets – that is, interpretation of presence of mitral regurgitation and/or aortic insufficiency on hand-held echocardiography that was not present on standard echocardiography – was the most common reason for non-agreement between hand-held and standard echocardiography interpretations. The expertise of the reader and the length of the protocol impacted the frequency of this finding. Non-experts receiving the focussed hand-held protocol made the error most commonly with 71/136 false-positive studies, representing 52%, followed by experts receiving the focussed hand-held protocols with 16/53, representing 30%, and experts receiving the complete hand-held protocol for review with 1/39 false-positive studies, representing 2.6% (Fig 7). The second most common source of false-positive studies came from the appropriate use of the simplified hand-held echocardiography criteria of mitral regurgitation ⩾1.5 cm or any aortic insufficiency compared with the more stringent published World Heart Federation diagnostic criteria of mitral regurgitation ⩾2.0 cm or aortic insufficiency ⩾1.0 cm, which accounted for the majority of other over-diagnoses.

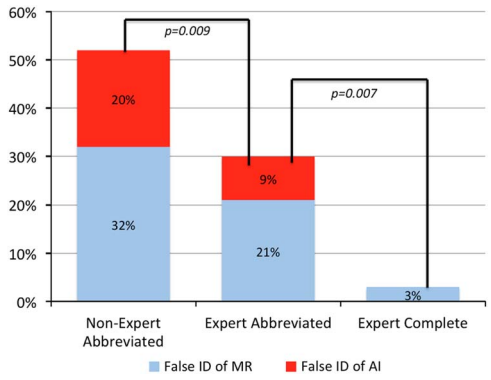

Figure 7.
Reasons for non-agreement – false-positive studies – between pooled reading groups and standard portable echocardiography interpretations. AI = aortic insufficiency; MR = mitral regurgitation.

The most common reasons for false-negative studies were lack of recognition of mitral regurgitation and/or aortic insufficiency on hand-held echocardiography, which was present on standard echocardiography with 39/115 false-negative interpretations, representing 34%, and in mitral regurgitation jet lengths that appeared shorter on hand-held compared with standard echocardiography imaging with 76/115 false-negative interpretations, representing 66%. No differences in reasons for false-negative studies were seen between reviewers or protocols.

Discussion

The previous work by our team and others has validated the utility of hand-held echocardiography performed by non-experts focussed on identifying well-defined color Doppler jets of mitral and aortic regurgitation to be a feasible approach to front-line

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screening for rheumatic heart disease in endemic regions.[9–11,13,19–23] Rheumatic heart disease is uniquely suited to benefit from this strategy, because it's morbidity and mortality is unacceptable,[24] it is highly endemic in regions of the world with limited healthcare resources, it is preventable with early detection, and because it has well-defined diagnostic criteria for latent disease that are solely based on echocardiography.[16] Optimal simplification of screening protocols has the potential to maximise the number of healthcare workers trained and children screened. This retrospective study builds on previous work, providing novel data supporting the feasibility of a single-view screening protocol for rheumatic heart disease that could meet this goal, paving the way for a prospective study to determine the true value of a single-view protocol.

Our study shows that in comparison with the gold-standard diagnosis using standard portable echocardiography imaging with 2012 World Heart Federation criteria,[16] a focussed hand-held echocardiography protocol that includes a single view – parasternal long axis – and a single measurement – mitral regurgitation length – has good sensitivity and negative predictive value for rheumatic heart disease screening both in the hands of expert and non-expert readers. In addition, there was no difference in sensitivity between experts interpreting complete hand-held protocols in three views and those interpreting focussed hand-held protocols, suggesting no benefit for case detection with more extended image acquisition.

The sensitivity of the focussed protocol was similar to that in previous reports of hand-held echocardiographic imaging and more complete image acquisition protocols using 13–15 images in the hands of non-experts. A total of three studies utilising these criteria in Uganda, Brazil, and Fiji – criteria of mitral regurgitation $\geqslant$1.5 cm or any aortic insufficiency – reported between 74.4 and 83% sensitivity.[12,13,25] As was seen in the current study, sensitivity in these studies increased to near 100% when restricted to cases of definite rheumatic heart disease.

The focussed hand-held protocol did result in lowered specificity and positive predictive value, though the majority of this difference was attributable to non-expert readers, with a non-significant difference in specificity observed between expert readers with the complete hand-held protocol and expert readers with the focussed hand-held protocol (90 versus 86.1%). As this study did not have a non-expert group receiving complete hand-held protocols, direct comparison of these two scenarios was not possible; however, the 75.4% specificity seen compares with the 78.8% specificity seen previously in Uganda,[12] but is lower than the 85–93% specificity seen from the Brazilian and Fijian non-expert cohorts.[13,25]

The goal of any screening process is to prioritise achieving a very low rate of false-negative studies while minimising false-positive studies. In our study, the negative predictive value of a screen-negative study for non-experts using the focussed hand-held protocol approached 100% under real-world field conditions and for definite rheumatic heart disease. This supports the value of using this protocol in a low-resource field setting, where uniform rapid screening with limited training could be implemented with a high likelihood of not missing positive cases. We acknowledge that this approach mandates a back-up system for positive studies and that it can inflate the number of patients referred for standard echocardiograms, potentially to the point of stressing local capacity to provide this service in low- and middle-income countries. It is likely that a single standard for simplified criteria will not fit all settings, and training protocols should consider local disease patterns and the ability of the health system to handle false-positive referrals. A sample screening policy algorithm using the focussed hand-held protocol is provided in Figure 8.

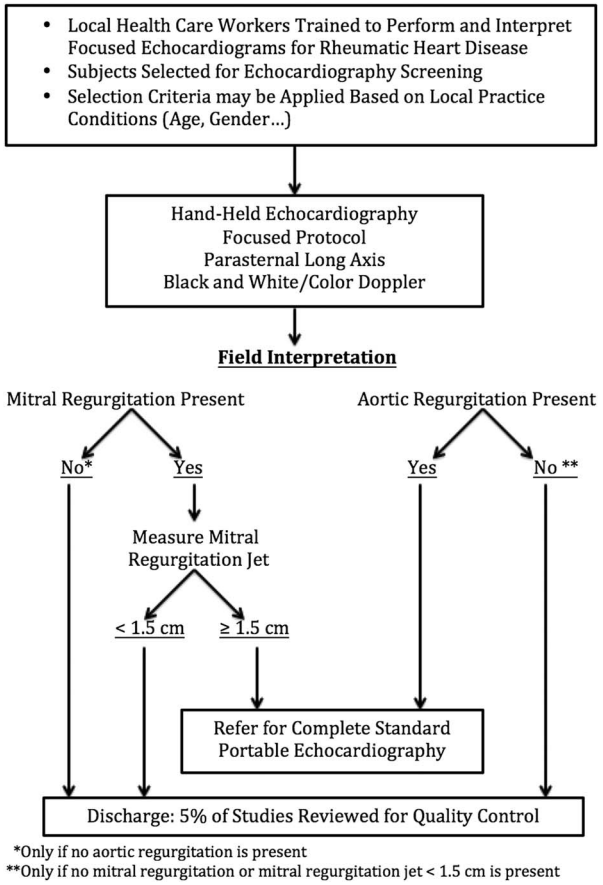

Figure 8.
Focussed hand-held echocardiography protocol sample algorithm

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Analysis of reasons for non-agreement between focussed non-expert hand-held echocardiography interpretation and standard portable echocardiography imaging suggests that erroneous identification of colour jets are the most common reasons for false-positive studies. Erroneous identification of colour mitral regurgitation or aortic insufficiency jets was least likely in experts reviewing complete hand-held images, more common in experts reviewing focussed hand-held images, and most frequent among non-experts reviewing focussed hand-held images. The error may be explained, in part, by the physics of color Doppler. When the expected mitral regurgitation colour jet is perpendicular to the angle of interrogation, which is true for parasternal long-axis but not for apical imaging, the other normal colour signals such as pulmonary vein inflow are more likely to be falsely identified as mitral regurgitation. Similarly, swirling of blood in the left ventricular outflow tract can be difficult to distinguish from aortic insufficiency, which becomes obvious in the apical views in which the aortic insufficiency jet is more distinctive and always moving towards the transducer.[26,27] As hand-held echocardiography machines do not have spectral Doppler, confirmation of pathological regurgitation using peak velocity (>3 m/second) and duration, (pansystolic – mitral regurgitation or pandiastolic – aortic insufficiency), two confirmatory features built into World Heart Federation criteria is not possible. Targeted training should emphasise other features of a high-velocity regurgitant jet, such as a mosaic colour pattern and the persistence of the jet through at least two frames, to improve specificity.

The majority of studies examining task shifting for rheumatic heart disease screening have utilised a combination of computer-based modules and hands-on training, which has lasted between 1 and 8 weeks.[9,12,13,25] Limiting the rheumatic heart disease screening protocol to a single view and measurement could accelerate this process and potentially lead to less variability in performance. Apical four-chamber views may be more challenging to obtain than parasternal long-axis views secondary to body habitus, breast tissue, and patient positioning. For this reason, utilisation of apical views requires longer hands-on training. In the only study that assessed the preference of non-experts, Mark et al[14] reported that emergency medicine faculty, fellows, and residents preferred the parasternal long-axis to other views when performing bedside ultrasound for assessment of left ventricular function.

Achieving uniform competency with training is also of critical importance if rheumatic heart disease screening is conducted on a larger scale. Studies that have reported individual trainees' performance, including this one, have shown a high degree of variability between non-experts who have undergone the same training.[13,25] Focussed single-view protocols could simplify training and facilitate the development of international standards, competency testing, and continuing education as advocated by The American Society of Echocardiography and the European Society of Cardiology.[28,29]

Another source of decrease in specificity comes from the appropriate application of the simplified hand-held echocardiography criteria of mitral regurgitation $\geqslant$1.5 cm or any aortic insufficiency compared with the more stringent published World Heart Federation diagnostic criteria of mitral regurgitation $\geqslant$2.0 cm or aortic insufficiency $\geqslant$1.0 cm, which was the second most common reason for "false-positive" studies in this cohort. It is important to remember that the proposed hand-held protocol is not meant for final rheumatic heart disease diagnosis. Hand-held echocardiography lacks spectral Doppler, which is needed to fulfil World Heart Federation criteria, and our hand-held protocols do not include assessment of the morphological features of the World Heart Federation criteria. Most believe that use of these morphological criteria for interpretation is too complex for non-experts carrying out field screening.[22] False-positive screening studies that occur secondary to proper use of simplified guidelines cannot be avoided, and complete confirmatory echocardiographies should be performed when possible. Although some authors have found acceptable sensitivity with a more stringent screening cut-off point of mitral regurgitation $\geqslant$2.0 cm or any aortic insufficiency,[9] others have found that this modification results in unacceptable loss of sensitivity,[10,12,13,25,30] and yet others have found even less stringent criteria of any mitral regurgitation or aortic insufficiency to be preferable.[25]

Our study builds on a previous study that assessed single-view long-axis imaging for rheumatic heart disease detection. Zuhlke et al reported that a single long-axis view had reasonable sensitivity (80.8%) and excellent specificity (100%) for rheumatic heart disease detection utilising the criteria of mitral regurgitation $\geqslant$2.0 cm.[31] The lower specificity seen in our study resulted from lowered mitral regurgitation jet length requirements (1.5 versus 2.0 cm), the inclusion of a varied and large group of nine reviewers – three of whom were non-experts – in contrast to a single expert reviewer, and the use of consensus standard echocardiography interpretations, again, from separate reviewers compared with the same reviewer. In addition, our study was powered to produce narrow confidence intervals, with 1761 studies reviewed, whereas this initial review of a focussed protocol included only 27 patients with rheumatic heart disease and 66 healthy controls.

Limitations

This was a retrospective study, and images were obtained as part of a more complete protocol. It is possible that prospective use of the focussed protocol could have higher sensitivity, as imagers would know that the single view was the only opportunity to look for regurgitation; however, performance in the field may be adversely impacted by additional challenges with image acquisition and the need to simultaneously acquire and interpret images. In addition, images were taken from previous studies; nine different individuals, some expert and some non-expert, obtained them in many different clinical settings including clinics, primary schools in Uganda, and primary schools in Brazil. We did not analyse the original imager or place of imaging to see whether there were differences. In some ways this heterogeneity provides an advantage, as it may make our results more generalisable. Our non-experts were also not completely new to image interpretation. All three were part of an ongoing rheumatic heart disease outreach team in Brazil, with 12–18 months of image acquisition and interpretation experience.[8] Thus, our results need to be replicated in new users undergoing training for the first time in a prospective study. Although we attempted to simulate "real-world" conditions with our low-prevalence group, group C, we expectedly have wide confidence intervals and lower positive predictive value, and a larger field validation of a focussed single-plane imaging protocol by non-experts using hand-held echocardiography should be considered.

Our study is limited to the use of the published World Heart Federation Guidelines[16] that use mitral regurgitation jet length as the cut-off point for screen-positive or screen-negative studies. Although flow convergence and contracting vein characteristics along with jet area provide more insight into severity of mitral regurgitation than jet length,[32] it would be challenging to incorporate more advanced color Doppler assessment tools into rheumatic heart disease screening protocols. More detailed comparison of the colour jet angle of interrogation and other characteristics between hand-held and standard portable echocardiography images would provide additional insight into the limitations of our focussed hand-held protocol and opportunities for improved education. This was beyond the scope or our retrospective design but could be incorporated into a prospective study.

Conclusion

Rheumatic heart disease screening through echocardiography may represent an important tool in reducing the global burden of rheumatic heart disease. True scaling of echocardiographic screening will best be carried out through vertical programming, and modifications of screening protocols that increase the speed and lessen the burden of training could improve the feasibility of integration into existing healthcare structures. A highly focussed single-view hand-held echocardiography protocol has good sensitivity and a high negative predictive value for rheumatic heart disease screening both in the hands of expert and non-expert readers and could be the next step in the evolution of rheumatic heart disease echocardiography. Further research should focus on replication across a variety of settings, refinement and decentralisation of training, and on the performance of this protocol in integrated healthcare projects.

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Conflicts of Interest

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the national guidelines on human experimentation of the United States, Brazil, and Uganda, and with the Helsinki Declaration of 1975, as revised in 2008. This work has been approved by the Institutional Review Boards of Children's National Medical Center, Makerere University School of Medicine, and Faculdade de Medicina da Universidade Federal de Minas Gerais.

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